CORRESPONDENCE

Association between rural residency, group D streptococcal endocarditis and colon cancer?

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We read with interest the article in *CMI* by Giannitsioti *et al.* [1] that analysed the link between rural residency and a higher proportion of group D streptococcal infective endocarditis (GDS IE).

In the last 20 years (1988–2007), we have diagnosed 68 cases of GDS IE, with 44 (64.7%) of these cases occurring in the last 6 years. These cases comprised 26% of the total number of cases of infective endocarditis (IE), and were associated with biotype I and colon tumours in 95% and 57% of patients, respectively. In total, 56% of the patients with GDS IE resided in rural areas, as compared to 35.6% of the 45 patients diagnosed with IE caused by viridans group streptococci during the same period ($p < 0.02$). Group D streptoccus was the primary cause of IE in our centre, with a high and increasing incidence. This, together with a greater frequency in rural areas, is very similar to the situation reported in France. However, overall, group D streptococcus constitutes a relatively infrequent cause of IE in Spain, perhaps because the majority of reports come from urban areas such as Madrid and Barcelona [2,3].

The association between rural residency and a higher incidence of GDS IE might be attributed, at least in part, as suggested by Giannitsioti *et al.* [1], to environmental factors, including dietary habits or contact with animals. Group D streptococcus is an intestinal bacterium that is isolated frequently from human specimens, as well as from the faeces of calves, young cattle and dairy cows [4]. Our region is one of the major areas in Spain for the production of cattle and dairy products, and the majority of the population lives in the countryside in close contact with cattle. Perhaps the local population has a higher rate of group D streptococcus faecal carriage, which, in combination with other factors that have been insufficiently researched, e.g., a change in the virulence of certain strains, changes in dietary habits, and an elderly population with a high number of degenerative valvulopathies, could favour this high incidence of IE.

Another question is whether these environmental factors might be associated with a higher incidence of colon tumours in these patients, given the association of this cancer with bacteraemia caused by *Streptococcus bovis* biotype I [5]. Accordingly, we analysed 130 cases of bacteraemia caused by group D streptococcus (with and without IE) according to biotype and rural residency. Eighty-nine involved biotype I (53% with colon cancers), and 41 involved biotype II (7% with colon cancers, $p < 0.0001$). However, rural residency was significantly more frequent in patients with biotype II (80.5% vs. 47%, $p < 0.0001$). Further epidemiological research is needed to explain these findings.

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REFERENCES

1. Giannitsioti E, Chirouze C, Bouvet A *et al.* Characteristics and regional variations of group D streptococcal endocarditis in France. *Clin Microbiol Infect* 2007; **13**: 770–776.
2. Bouza E, Menasalvas A, Muñoz P, Vasallo FJ, Moreno MM, García MA. Infective endocarditis—a prospective study at the end of the twentieth century: new predisposing conditions, new etiologic agents, and still a high mortality. *Medicine (Baltimore)* 2001; **80**: 298–307.
3. Tornos P, Permanyer-Miranda G, Olona M *et al.* Long-term complications of native infective endocarditis in non-addicts. A 15-year study. *Ann Intern Med* 1992; **117**: 567–572.
4. Devriese L, Laurier L, De Herdt P, Haesebrouck F. Enterococcal and streptococcal species isolated from faeces of calves, young cattle and dairy cows. *J Appl Bacteriol* 1992; **72**: 29–31.
5. Corredoira J, Alonso MP, García JF *et al.* Clinical characteristics and significance of *Streptococcus salivarius* bacteremia and *Streptococcus bovis* bacteremia: a prospective 16-year study. *Eur J Clin Microbiol Infect Dis* 2005; **24**: 250–255.

In-vitro activity and in-vivo efficacy of catheters impregnated with chloroxylenol and thymol against uropathogens

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Further to our recent publication in CMI describing the antifungal activity of urinary catheters impregnated with chlorhexidine and chloroxylenol [1], we would like to report some additional data concerning other antimicrobial options. Urinary tract infection, which is often associated with an indwelling bladder catheter, accounts for

Table 1. In-vitro zones of inhibition against uropathogens (mm)

Organism	Baseline	3 days	7 days	14 days
Klebsiella pneumoniae	27	28	25	22
Pseudomonas aeruginosa	14	13	15	9
Escherichia coli	26	22	27	21
Citrobacter diversus	26	26	23	17
Enterobacter cloacae	37	35	32	33
Proteus mirabilis	35	36	30	30
Staphylococcus aureus (MRSA)	39	40	38	42
Enterococcus faecium	48	49	46	36
Enterococcus faecalis	30	27	28	24
Candida albicans	53	46	42	36

MRSA, methicillin-resistant *S. aureus*.

c. 40% of all nosocomial infections [2]. The pathogenesis of catheter-associated urinary tract infection generally starts with colonisation of the surface of an indwelling catheter and the formation of a biofilm that shelters sessile bacteria from systemic antibiotics. Most previous approaches utilising antimicrobial agents have failed to demonstrate significant clinical protection against infection [3]. In addition, the anti-infective activity of many currently available antimicrobial-associated urinary catheters is limited in terms of durability and spectrum of activity [3,4].

To expand our previous work, 16 French silicone urinary catheters were impregnated with a solution of chloroxylenol (CX) 150 mg/mL and thymol (TH) 400 mg/mL, and then gas-sterilised, as described previously [1]. CX and TH have been used clinically for pre-surgery skin preparation and as an oral antiseptic, respectively [5,6]. The in-vitro antimicrobial activity of CX/TH-impregnated 2-cm catheter segments was then investigated at baseline, and at 3, 7 and 14 days after suspension in synthetic urine [7], by determining the zones of inhibition [8] against ten clinical isolates (including Gram-positive cocci, Gram-negative bacilli and *Candida*) responsible for clinical episodes of infection. The zones of inhibition observed (Table 1) demonstrated broad-spectrum activity of the antimicrobial-impregnated catheters against all ten organisms tested. No zone of inhibition was observed around control catheter segments against any of the organisms tested.

The concentrations of CX and TH on impregnated catheter segments were determined using HPLC. CX and TH were acetone-extracted, in duplicate, from individual 1-cm catheter segments, and lyophilised extracts were subsequently reconstituted in HPLC buffer consisting of methanol:water (75:25). Individual samples were tested in a reversed-phase HPLC system using a C18 column with a modified flow rate of 2.5 mL/min isocratically as described previously [9]. HPLC analysis indicated that a 1-cm segment of antimicrobial-impregnated urinary catheter contained an average of 1.4 mg of CX and 4.2 mg of TH.

After securing approval from the Institutional Animal Care and Use Committee, the in-vivo efficacy of antimicrobial-impregnated catheters was assessed using a previously described animal model [1,10]. In total, 32 2-cm catheter segments were placed in the backs of eight female New Zealand White specific pathogen-free rabbits (two antimicrobial-impregnated and two non-impregnated catheter segments per rabbit). Each device was inoculated with 10^5 ***CFU of*** *Enterobacter cloacae*, and the wounds were then sutured. After 1 week, the rabbits were humanely killed and the catheter segments were removed and cultured [11,12]. Device colonisation was defined as growth of *E. cloacae* from catheter cultures. The in-vivo results indicated that only 2/16 (12.5%) antimicrobial-impregnated catheters became colonised with *E. cloacae*, compared with 10/16 (62.5%) of the control catheters (p 0.009). Blood cultures obtained before the animals were killed were negative for all eight rabbits.

Although some surface-modified urinary catheters described previously have been found to delay the onset of bacteriuria, none has been shown in a prospective randomised clinical trial to have broad-spectrum and durable efficacy in preventing clinical episodes of catheter-associated urinary tract infection [4,13]. The present results indicate that urinary catheters impregnated with CX and TH provide durable broad-spectrum antimicrobial activity, and previous studies have indicated that in-vitro zones of inhibition ≥10–15 mm may predict in-vivo efficacy in animal models [10], which is in agreement with the findings of the present in-vivo animal study. However, additional studies are still required to assess the safety and efficacy of this approach.

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REFERENCES

1. Darouiche RO, Mansouri MD, Kojic EM. Antifungal activity of antimicrobial-impregnated devices. *Clin Microbiol Infect* 2006; **12**: 397–399.
2. Warren JW. The catheter and urinary tract infection. *Med Clin North Am* 1991; **75**: 481–493.
3. Maki D, Tambyah P. Engineering out the risk of infection with urinary catheters. *Emerg Infect Dis* 2001; **7**: 1–13.
4. Brosnahan J, Jull A, Tracy C. Types of urethral catheters for managment of short-term voiding problems in hospitalised adults (Cochrane Review). In: *The Cochrane Library*, issue 2. Oxford: Update Software, 2004.
5. Ostrander RV, Botte MJ, Brage ME. Efficacy of surgical preparation solutions in foot and ankle surgery. *J Bone Joint Surg Am* 2005; **87**: 980–985.
6. Kasuga Y, Ikenoya H, Okuda K. Bactericidal effects of mouth rinses on oral bacteria. *Bull Tokyo Dent Coll* 1997; **38**: 297–302.
7. Minuth JN, Musher DM, Thorsteinsson SB. Inhibition of the antibacterial activity of gentamicin by urine. *J Infect Dis* 1976; **133**: 14–21.
8. Sherertz RJ, Forman DM, Solomon DD. Efficacy of dicloxacillin-coated polyurethane catheters in preventing subcutaneous *Staphylococcus aureus* infection in mice. *Antimicrob Agents Chemother* 1989; **33**: 1174–1178.
9. Thompson RD, Carlson M. Determination of thymol in halothane anaesthetic preparations by high-performance liquid chromatography. *J Pharm Biomed Anal* 1989; **7**: 1199–1206.
10. Sherertz RJ, Carruth WA, Hampton AA, Byron MP, Solomon DD. Efficacy of antibiotic-coated catheters in preventing subcutaneous *Staphylococcus aureus* infection in rabbits. *J Infect Dis* 1993; **167**: 98–106.
11. Sherertz JR, Raad II, Belani A *et al.* Three-year experience with sonicated vascular catheter cultures in a clinical microbiology laboratory. *J Clin Microbiol* 1990; **28**: 76–82.
12. Raad II, Hanna HA, Darouiche RO. Diagnosis of catheter-related bloodstream infections: is it necessary to culture the subcutaneous catheter segment? *Eur J Clin Microbiol Infect Dis* 2001; **20**: 556–558.
13. Trautner BW, Darouiche RO. Catheter-associated infections: pathogenesis affects prevention. *Arch Intern Med* 2004; **164**: 842–850.